I hereby certify that this correspondence is being electronically transmitted to the United States Patent and Trademark Office on the date shown below:

March 3, 2008.

David Saliwanchik

David R. Saliwanchik, Patent Attorney

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322
Docket No. CHROM-3XC1
Patent No. 7,317,111

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Ram Bhatt, Michael J. Conrad, Azzouz Bencheikh, Yifeng Xiong
Issued	:	January 8, 2008
Patent No.	:	7,317,111
For	:	Novel Green and Orange Fluorescent Labels and Their Uses

Mail Stop Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 CFR 1.322 (OFFICE MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

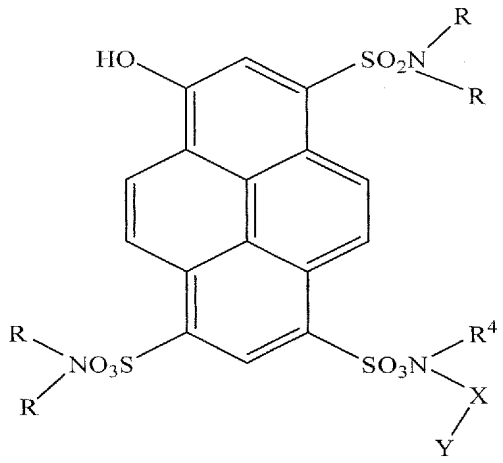
In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:	**Application Reads:**
Cover Page, Item 75, Lines 3-4:	Page 3 of the Declaration under 37 CFR 1.63 and Power of Attorney ("Residence" for "Azzouz Bencheikh"):
"San Diego, CA"	--Rancho Santa Fe, California--

Patent Reads:

Column 11, Line 30:

"



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Application Reads:

Page 16 of the Specification, Structure II :

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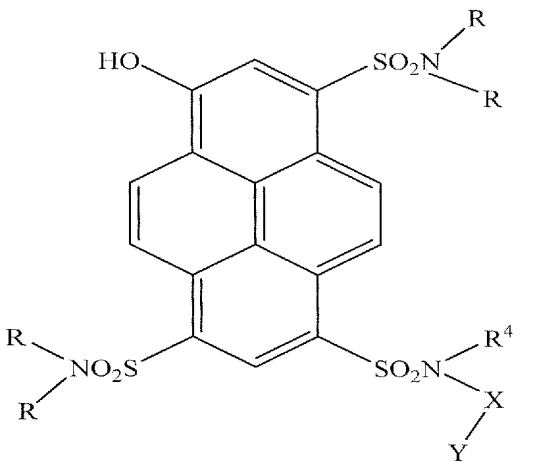

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Column 11, Table 1, Line 58:

"-SH, -NH_2, -NCS, -NCO,."

Page 17 of the Specification, Table 1, Column R2:

---SH, -NH_2, -NCS, -NCO,--

Column 19, Line 41:

"λ ex = 490 run"

Page 28 of the Specification, Line 23:

--λ ex = 490 nm--

Column 23, Line 23:

"GCT.GCT.GCA.GGT.CGA.GAA.GGC.TTC"

Page 33 of the Specification, Line 20:

--GCT.GCA.GGT.CGA.GAA.GGC.TTC--

True and correct copies of the Declaration under 37 CFR 1.63 and Power of Attorney and pages 16, 17, 28, and 33 of the specification as filed which support Applicants' assertion of the errors on the part of the Patent Office accompanies this Certificate of Correction.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,

David Saliwanchik

David R. Saliwanchik
Patent Attorney
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Gainesville, FL 32614-2950

DRS/yvs

Attachments: Certificate of Correction
Declaration under 37 CFR 1.63 and Power of Attorney
Pages 16, 17, 28, and 33 of the specification as filed

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,317,111 Page 1 of 2

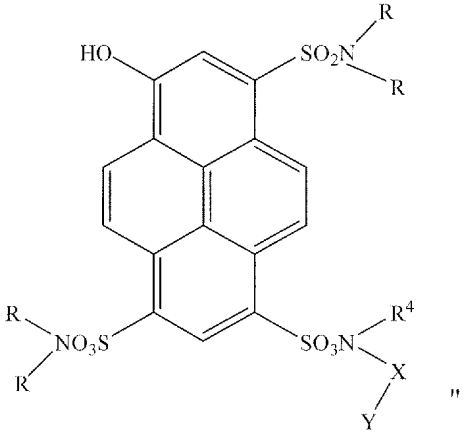
DATED : January 8, 2008

INVENTORS : Ram Bhatt, Michael J. Conrad, Azzouz Bencheikh, Yifeng Xiong

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Cover Page,
Item 75, Lines 3-4, "San Diego, CA" should read --Rancho Santa Fe, CA--.

Column 11,
Line 30, should read:
"



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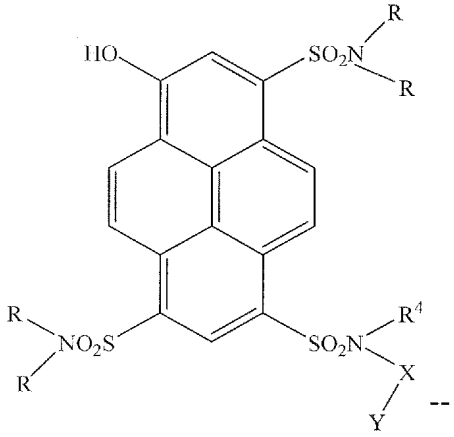

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,317,111

DATED : January 8, 2008

INVENTORS : Ram Bhatt, Michael J. Conrad, Azzouz Bencheikh, Yifeng Xiong

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Table 1, Line 58, "-SH, -NH_2, -NCS, -NCO,." should read ---SH, -NH_2, -NCS, -NCO,--.

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Line 41, "λ ex = 490 run" should read --λ ex = 490 nm--.

Column 23,
Line 23, "GCT.GCT.GCA.GGT.CGA.GAA.GGC.TTC" should read
--GCT.GCA.GGT.CGA.GAA.GGC.TTC--.

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PTO/SB/05 (11-00)
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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	CHROM-3XC1
First Inventor	Ram Bhatt
Title	Novel Green and Orange Fluorescent Labels and Their Uses
Express Mail Label No.	EU 082848728 US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. [✔] Fee Transmittal Form (e.g., PTO/SB/17) *(Submit an original and a duplicate for fee processing)*
2. [✔] Applicant claims small entity status. See 37 CFR 1.27.
3. [✔] Specification [*Total Pages* 56] *(preferred arrangement set forth below)*
   - Descriptive title of the invention
   - Cross Reference to Related Applications
   - Statement Regarding Fed sponsored R & D
   - Reference to sequence listing, a table, or a computer program listing appendix
   - Background of the Invention
   - Brief Summary of the Invention
   - Brief Description of the Drawings (*if filed*)
   - Detailed Description
   - Claim(s)
   - Abstract of the Disclosure
4. [✔] Drawing(s) *(35 U.S.C. 113)* [*Total Sheets* 23]
5. Oath or Declaration [*Total Pages* 3]
   a. [ ] Newly executed (original or copy)
   b. [✔] Copy from a prior application (37 CFR 1.63 (d)) *(for continuation/divisional with Box 18 completed)*
      i. [ ] DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).
6. [ ] Application Data Sheet. See 37 CFR 1.76

ADDRESS TO: Assistant Commissioner for Patents
Box Patent Application
Washington, DC 20231

7. [ ] CD-ROM or CD-R in duplicate, large table or Computer Program (*Appendix*)
8. Nucleotide and/or Amino Acid Sequence Submission (*if applicable, all necessary*)
   a. [ ] Computer Readable Form (CRF)
   b. Specification Sequence Listing on:
      i. [ ] CD-ROM or CD-R (2 copies); or
      ii. [ ] paper
   c. [ ] Statements verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

9. [ ] Assignment Papers (cover sheet & document(s))
10. [ ] 37 CFR 3.73(b) Statement *(when there is an assignee)* [ ] Power of Attorney
11. [ ] English Translation Document *(if applicable)*
12. [ ] Information Disclosure Statement (IDS)/PTO-1449 [ ] Copies of IDS Citations
13. [ ] Preliminary Amendment
14. [✔] Return Receipt Postcard (MPEP 503) *(Should be specifically itemized)*
15. [ ] Certified Copy of Priority Document(s) *(if foreign priority is claimed)*
16. [ ] Request and Certification under 35 U.S.C. 122 (b)(2)(B)(i). Applicant must attach form PTO/SB/35 or its equivalent.
17. [✔] Other: Certificate of Mailing by Express Mail

18. If a CONTINUING APPLICATION, *check appropriate box, and supply the requisite information below and in a preliminary amendment, or in an Application Data Sheet under 37 CFR 1.76:*

[ ] Continuation [ ] Divisional [ ] Continuation-in-part (CIP) of prior application No.: _____/_____

Prior application information: *Examiner* _____ *Group Art Unit:* _____

For CONTINUATION OR DIVISIONAL APPS only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 5b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation can only be relied upon when a portion has been inadvertently omitted from the submitted application parts.

19. CORRESPONDENCE ADDRESS

[✔] *Customer Number or Bar Code Label* 23,557 or [ ] *Correspondence address below*

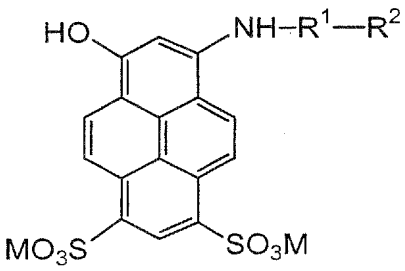
Name					
Address					
City		*State*		*Zip Code*	
Country		*Telephone*		*Fax*	

Name (Print/Type)	Margaret Efron	*Registration No. (Attorney/Agent)*	47,545
Signature		*Date*	09/23/03

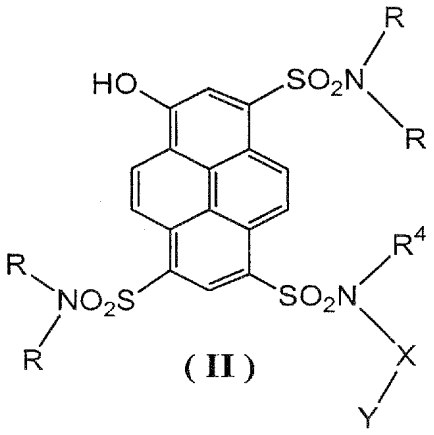
Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231.

their distal ends and through which the fluorophore can be covalently attached as a fluorescent label to another, non-fluorescent molecule such as a protein, oligonucleotide, lipid, small molecule ligand or a peptide.

In a preferred embodiment, the substrates of the subject invention have the general formula represented by the structures (I) or (II) :



(I)



(II)

where R^1, R^2, X and Y represent spacers and conjugating linkers of different compositions, and where R and R^4 are hydrogen, alkyl or phenyl substituents. Specific examples are shown in the following tables.

Table 1. Spacers and Linkers associated with the compounds of Structure I	
R1	**R2**
CO – (CH_2)n where n = 1-15	- COOH, - SH, -NH_2, -NCS, -NCO, - CO_2-NHS, - Maleimide
- CO- PEG	- COOH, - SH, -NH_2, -NCS, -NCO, - CO_2-NHS, - Maleimide
- CO- DEXTRAN	- COOH, - SH, -NH_2, -NCS, -NCO, - CO_2-NHS, - Maleimide
$CO(CH_2)n$-$(CONHCHCONH)_N$ | R n = 1-15 R = Alkyl, Aryl N = 1 -100	- COOH, - SH, -NH_2, -NCS, -NCO, - CO_2-NHS, - Maleimide
CO- Aryl-$(CH_2)_n$ n= 1-15	- COOH, - SH, -NH_2, -NCS, -NCO, - CO_2-NHS, - Maleimide
CO $(CH_2)_n$ – CONH-$(CH_2)_N$- n= 1-15, N= 1-15	- SH, -NH_2, -NCS, -NCO, - Maleimide, -NHNH2
CO (CH_2)n- CONH- PEG n = 1-15	- SH, -NH_2, -NCS, -NCO, - Maleimide, -$NHNH_2$
CO (CH_2)n- CONH- DEXTRAN n = 1-15	- SH, -NH_2, -NCS, -NCO, - Maleimide, -$NHNH_2$
CH_2- (CH_2)n- CONH- X Where X = (CH_2)n , n = 1-15 = PEG = Dextran CH_2-$(CH_2)_n$	- SH, -NH_2, -NCS, -NCO, COONHS, - Maleimide, -$NHNH_2$
CH_2-(CH_2)n n = 1-15	- SH, -NH_2, -NCS, - Maleimide, COONHS

Example 11 — 1-Hydroxy-3,6-di-(dimethylsulfonamido)-8-(3-aminopropyl-methyl-sulfonamido)-pyrene (compound 15)

To chlorosulfonic acid (8 ml) was added compound **14** (940 mg, 1.83 mMol) at room temperature. The mixture was stirred at room temperature over the weekend and quenched with ice carefully. The solid was filtered off, dried on the vacuum for 30 min. This was added to a solution of N-methyl-3-amino-propane (2M in THF, 20 ml) in acetone (5 ml). The resulting mixture was stirred for 1 h and concentrated in *vacuo*. Flash chromatography on a silica gel column using $CHCL_3$-MeOH (4:1) provided the desired product **15** as a yellow solid (540 mg, 50%). ^{1}H NMR (DMSO, 500 mHz): 1.85-1.90 (m, 2H), 2.65-2.83 (m, 12H), 2.89 (s, 3H), 3.30-3.36 (m, 6H), 8.0 (s, 1H), 8.25-8.28 (m, 1H), 8.80-8.90 (m, 3H), 8.97-9.0 (m, 1H); MS (M-H): 581; fluorescence (MeOH/H_2O): λ ex = 490 nm, λ em = 548 nm.

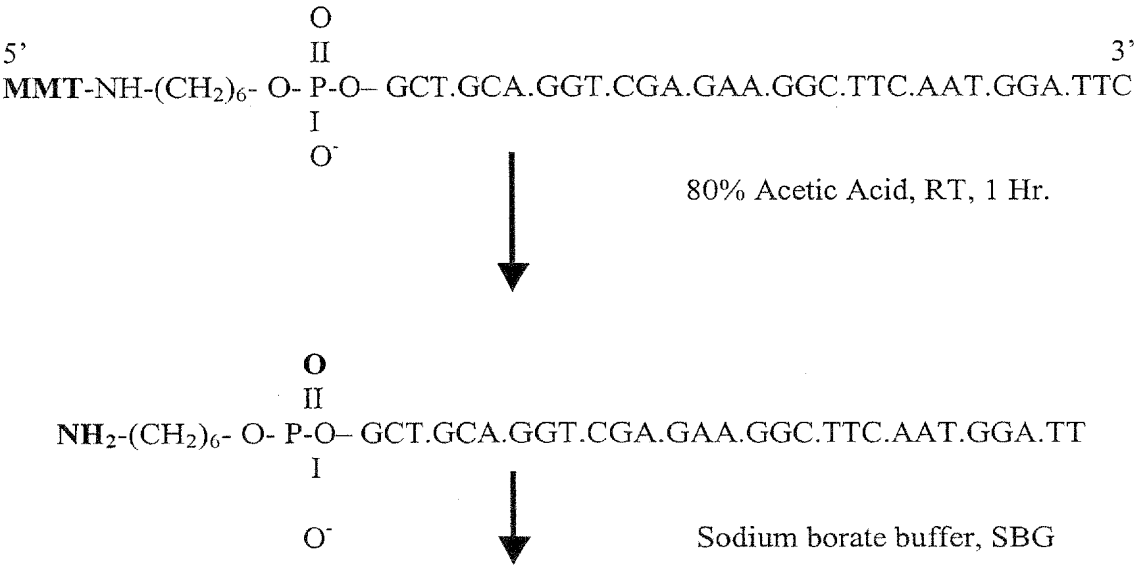
Example 12 — 1-Hydroxypyrene-3,6-di-(dimethylsulfonamido)-8-(3-isothiocyanato-propyl-methylsulfonamide (compound 16)

To a solution of 15 (230 mg, 0.40 mMol) in DMF (8 ml) was added thiocarbonyl diimidazole (142 mg, 0.8 mMol). The mixture was stirred at room temperature for a few hours and concentrated in *vacuo*. Flash chromatography on silica gel column, as described above, provided StarBright **Orange**, compound **16** as a yellow solid (200 mg, 80%). ^{1}H NMR (DMSO, 500 mHz): 1.89 (t, 2H), 2.81-2.84 (m, 12H), 2.86 (s, 3H), 3.27 (t, 2H), 3.66 (t, 2H), 8.33 (s, 1H), 8.85 (d, 1H), 9.0 (s, 1H), 9.05 (d, 1H), 9.14 (d, 1H), 9.20 (d, 1H), 12.0 (s, br, 1H); MS (M-H): 623; fluorescence (MeOH/H_2O): λ ex = 490 nm, λ em = 548 nm.

Example 13 — 1-Hydroxy-3,6-di(dimethylsulfonamido)-8-(4'-succinimidylbutyrate)-phenylsulfonamido- pyrene (compound 17)

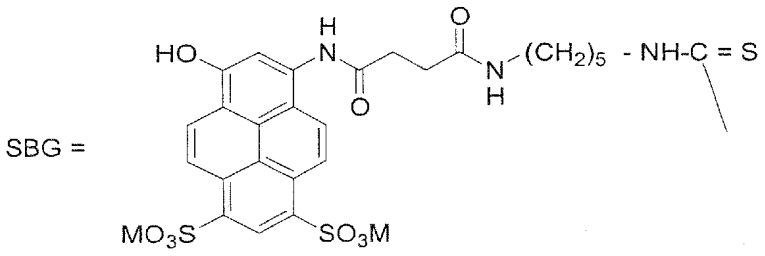
Compound **14** (550 mg, 1.07 mMol) was dissolved in chlorosulfonic acid (10 ml) and stirred at room temperature overnight. The resulting sulfonyl chloride was then precipitated on ice and the solid filtered off and washed with 2x 20 ml of cold water. This precipitated was then re-dissolved in 40 ml of dry THF and treated dropwise with a THF (10ml) solution of 4-aminophenyl Butyric acid (283 mg 2.14 mMol). The resulting dark orange solution was stirred at room temperature overnight

column using a linear gradient of 10% acetonitrile/ 0.1M TEAA to 100 % acetonitrile in 25 minutes (1 ml/ min.). The product peak was collected and concentrated to dryness to obtain the MMT-NH-oligonucleotide



6 SBG- NCS- NH- $(CH_2)_5$ -OPO_3-GCT.GCA.GGT. CGA.GAA. GGC.TTC. AAT.GGA.TT

The complete structure of SBG as attached to an oligonucleotide is shown below:



6

The MMT-NH –olignucleotide was treated with 80% acetic acid in water at RT for 1 hour to remove the MMT group to obtain free amino group at the distal end of the linker attached to the 5'-end of the oligonucleotide. After evaporating the acetic acid